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[Intervention Review]

Sucrose for analgesia in newborn infants undergoing painful procedures

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ABSTRACT

Background

Administration of oral sucrose with and without non-nutritive sucking is the most frequently studied non-pharmacological intervention for procedural pain relief in neonates.

Objectives

To determine the efficacy, effect of dose, method of administration and safety of sucrose for relieving procedural pain in neonates as assessed by validated composite pain scores, physiological pain indicators (heart rate, respiratory rate, saturation of peripheral oxygen in the blood, transcutaneous oxygen and carbon dioxide (gas exchange measured across the skin - TcpO₂, TcpCO₂), near infrared spectroscopy (NIRS), electroencephalogram (EEG), or behavioural pain indicators (cry duration, proportion of time crying, proportion of time facial actions (e.g. grimace) are present), or a combination of these and long-term neurodevelopmental outcomes.

Search methods

We used the standard methods of the Cochrane Neonatal. We performed electronic and manual literature searches in February 2016 for published randomised controlled trials (RCTs) in the Cochrane Central Register of Controlled Trials (CENTRAL; *The Cochrane Library*, Issue 1, 2016), MEDLINE (1950 to 2016), EMBASE (1980 to 2016), and CINAHL (1982 to 2016). We did not impose language restrictions.

Selection criteria

RCTs in which term or preterm neonates (postnatal age maximum of 28 days after reaching 40 weeks' postmenstrual age), or both, received sucrose for procedural pain. Control interventions included no treatment, water, glucose, breast milk, breastfeeding, local anaesthetic, pacifier, positioning/containing or acupuncture.

Data collection and analysis

Our main outcome measures were composite pain scores (including a combination of behavioural, physiological and contextual indicators). Secondary outcomes included separate physiological and behavioural pain indicators. We reported a mean difference (MD) or weighted MD (WMD) with 95% confidence intervals (CI) using the fixed-effect model for continuous outcome measures. For categorical data we used risk ratio (RR) and risk difference. We assessed heterogeneity by the I^2 test. We assessed the risk of bias of included trials using the Cochrane 'Risk of bias' tool, and assessed the quality of the evidence using the GRADE system.

Main results

Seventy-four studies enrolling 7049 infants were included. Results from only a few studies could be combined in meta-analyses and for most analyses the GRADE assessments indicated low- or moderate-quality evidence. There was high-quality evidence for the beneficial effect of sucrose (24%) with non-nutritive sucking (pacifier dipped in sucrose) or 0.5 mL of sucrose orally in preterm and term infants: Premature Infant Pain Profile (PIPP) 30 s after heel lance WMD -1.70 (95% CI -2.13 to -1.26; $I^2 = 0\%$ (no heterogeneity); 3 studies, $n = 278$); PIPP 60 s after heel lance WMD -2.14 (95% CI -3.34 to -0.94; $I^2 = 0\%$ (no heterogeneity); 2 studies, $n = 164$). There was high-quality evidence for the use of 2 mL 24% sucrose prior to venipuncture: PIPP during venipuncture WMD -2.79 (95% CI -3.76 to -1.83; $I^2 = 0\%$ (no heterogeneity); 2 groups in 1 study, $n = 213$); and intramuscular injections: PIPP during intramuscular injection WMD -1.05 (95% CI -1.98 to -0.12; $I^2 = 0\%$ (2 groups in 1 study, $n = 232$)). Evidence from studies that could not be included in RevMan-analyses supported these findings. Reported adverse effects were minor and similar in the sucrose and control groups. Sucrose is not effective in reducing pain from circumcision. The effectiveness of sucrose for reducing pain/stress from other interventions such as arterial puncture, subcutaneous injection, insertion of nasogastric or orogastric tubes, bladder catheterization, eye examinations and echocardiography examinations are inconclusive. Most trials indicated some benefit of sucrose use but that the evidence for other painful procedures is of lower quality as it is based on few studies of small sample sizes. The effects of sucrose on long-term neurodevelopmental outcomes are unknown.

Authors' conclusions

Sucrose is effective for reducing procedural pain from single events such as heel lance, venipuncture and intramuscular injection in both preterm and term infants. No serious side effects or harms have been documented with this intervention. We could not identify an optimal dose due to inconsistency in effective sucrose dosage among studies. Further investigation of repeated administration of sucrose in neonates is needed. There is some moderate-quality evidence that sucrose in combination with other non-pharmacological interventions such as non-nutritive sucking is more effective than sucrose alone, but more research of this and sucrose in combination with pharmacological interventions is needed. Sucrose use in extremely preterm, unstable, ventilated (or a combination of these) neonates needs to be addressed. Additional research is needed to determine the minimally effective dose of sucrose during a single painful procedure and the effect of repeated sucrose administration on immediate (pain intensity) and long-term (neurodevelopmental) outcomes.

PLAIN LANGUAGE SUMMARY

Sucrose for analgesia (pain relief) in newborn infants undergoing painful procedures

Review question

Cochrane reviewers investigated how well sucrose (table sugar) works as a reliever of pain in newborn babies who are having painful procedures (e.g. an injection, or heel lance, or insertion of a needle to obtain a blood sample (venipuncture), or eye examinations). The babies' pain responses (e.g. crying, grimacing) were assessed by scoring systems for pain used by health care professionals to measure the pain that babies are experiencing. In addition, the reviewers wanted to investigate whether the level of pain relief is related to the dose of sucrose, or the method of delivery (e.g. as a solution squirted into the mouth, or on a pacifier (also called a soother or dummy), and whether there are any safety concerns about using sucrose to relieve pain.

Background

Although there are ways to manage the pain of surgery, medical illness and major procedures, ways of preventing or reducing pain from minor medical procedures (e.g. heel lance and venipuncture) have, until relatively recently, been lacking. Sucrose has been examined for its calming effects in crying newborns and its pain-relieving effects for invasive procedures in full-term and premature newborns.

Study characteristics

We searched the medical literature widely up to February 2016 for studies that investigated the pain-relieving effect of sucrose for minor medical procedures in newborn full-term and premature babies. We included randomised controlled trials only, as these provide the most reliable medical evidence. We identified 74 studies that reported on a total of more than 7000 infants in this Cochrane Review.

Thirty-eight studies included full-term babies only, 31 included premature babies only, and five included both full-term and premature babies. Heel lance was the painful procedure in 38 studies, and venipuncture in nine; the remaining studies investigated a wide variety of other minor painful procedures.

The studies used a variety of delivery methods for the sucrose solution (oral syringe, dropper or sucrose-dipped pacifier), as well as a range of concentrations and volumes of dose. Sucrose treatment was compared with giving the babies a similar volume of water, a pacifier, routine care, breastfeeding, 'facilitated tucking' (holding the infant in a flexed position with arms close to the body and hands placed to promote sucking), laser acupuncture, swaddling, warmth, anaesthetic cream for the skin (EMLA), or a combination of these. The studies used a range of pain assessment scales to measure their results.

Study funding sources

We did not identify any studies that received funding from the industry.

Key results

There was high-quality evidence that sucrose reduces different measures of newborn pain during heel lance, venipuncture and intramuscular injection. However, sucrose does not provide effective pain relief during circumcision. There is conflicting evidence for whether sucrose reduces pain for other minor painful procedures and further research is needed to investigate these more thoroughly.

Twenty-nine studies reported on adverse events (harms of the sucrose and other treatments) and found that the number of minor adverse events (e.g. choking or gagging) was very low, and was similar in the different groups (so not attributable to the sucrose treatment). No major adverse events were reported.

Quality of evidence

Although sucrose has been widely studied as a pain reliever for newborn babies, most studies have included few babies and have used many different measures of pain to assess its effectiveness. We identified high-quality evidence that sucrose reduces pain for heel lance, venipuncture and intramuscular injection. The quality of evidence was low or moderate in favour for the use of sucrose for other painful procedures.